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Up front

Competition for publication in Diabetologia continues to grow, and less than 20% of papers are accepted. Of all the high-quality papers that appear in this month's issue I want to draw your attention to five articles that I think stand out in some regard and are very interesting. The articles are summarised here. Our publisher, Springer, has kindly made the full text of each of these papers freely available.
I hope you enjoy reading them!

Hindrik Mulder, Editor

Lipids, hyperreflective crystalline deposits and diabetic retinopathy: potential systemic and retinal-specific effect of lipid-lowering therapies

Alicia J. Jenkins, Maria B. Grant, Julia V. Busik

The highly metabolically active retina obtains crucial lipids through both endogenous biosynthesis and via the systemic circulation. Both quantitative and qualitative changes in lipids have been associated with diabetic retinopathy. Whilst the role of lipids and lipid-modifying drugs in cardiovascular disease in people with diabetes is well-studied, their roles in diabetic retinopathy are currently less well known. In this issue, Jenkins et al (https://doi.org/10.1007/s00125-022-05655-z) review the potential role of lipids and lipid-lowering drugs in diabetic retinopathy, examining results from retinal tissue analyses, clinical observational studies, clinical trials and meta-analyses. The authors discuss several statin and fibrate trials that were designed to predominantly address cardiovascular outcomes, but which have also reported potential retinal benefits. They outline the many challenges in this clinically important field, but also highlight the ongoing research in this area. This includes several in-progress trials of lipid drugs that have diabetic retinopathy-related primary endpoints, which may further elucidate the potential mechanisms by which lipid-modifying therapies could impact diabetic retinopathy. The figures from this review are available as a downloadable slideset.

Effectiveness of continuous glucose monitoring in maintaining glycaemic control among people with type 1 diabetes mellitus: a systematic review of randomised controlled trials and meta-analysis

Evelyn Teo, Norasyikin Hassan, Wilson Tam, Serena Koh

Glucose monitoring is a key method for individuals with type 1 diabetes to maintain adequate glycaemic control and delay the onset of diabetic complications. The limitations of traditional self-monitoring of blood glucose (SMBG) can be overcome by using continuous glucose monitoring (CGM). Current reviews regarding the effectiveness of CGM and SMBG on glycaemic control revealed several research gaps. In this issue, Teo et al (https://doi.org/10.1007/s00125-021-05648-4) report that CGM significantly reduces HbA_{1c} levels compared with SMBG, with larger effects observed among those with higher baseline HbA_{1c}. However, their results show that CGM has no effect on severe hypoglycaemia and diabetic ketoacidosis. The authors conclude that CGM is superior to SMBG in improving glycaemic control, especially among those with poorly controlled glycaemia. They also suggest that individuals with poorly controlled glycaemia would benefit most from CGM compared with SMBG in the community.

Understanding the pathogenesis of lean non-autoimmune diabetes in an African population with newly diagnosed diabetes

Davis Kibirige, Isaac Sekitoleko, William Lumu, Angus G. Jones, Andrew T. Hattersley, Liam Smeeth, Moffat J. Nyirenda

Atypical diabetes has been described in sub-Saharan Africa, with non-insulin-requiring apparent type 2 diabetes seen in lean and sometimes young individuals. However, robust data on the clinical and metabolic characterisation of these lean individuals with diabetes are lacking. In this issue, Kibirige et al (https://doi.org/10.1007/s00125-021-05644-8) investigate the phenotype of newly diagnosed adult-onset diabetes in Uganda. The authors report that individuals with a lean type 2 diabetes phenotype were predominantly male, exhibiting significant pancreatic beta cell dysfunction but no evidence of the metabolic syndrome or insulin resistance. This study further adds to evidence of differences in the pathogenesis of type 2 diabetes across populations. The authors suggest that due to the observed differences in underlying pathophysiological defects of type 2 diabetes, there is a need for interventional studies to investigate the optimal individualised therapies for individuals with a lean type 2 diabetes phenotype in sub-Saharan Africa.

Glucolipotoxicity promotes the capacity of the glycerolipid/NEFA cycle supporting the secretory response of pancreatic beta cells

Lucie Oberhauser, Cecilia Jiménez-Sánchez, Jesper Grud Skat Madsen, Dominique Duhamel, Susanne Mandrup, Thierry Brun, Pierre Maechler

About three decades ago, in the context of type 2 diabetes, the concept of lipotoxicity, and later of glucolipotoxicity, was applied to pancreatic beta cells. However, after all these years it remains debated whether essential components of the organ's chemistry, namely fat and sugar, could be qualified as genuine toxic molecules. In this issue, Oberhauser et al (https://doi.org/10.1007/s00125-021-05633-x) report results from a study in which they exposed pancreatic islets to various so-called glucolipotoxic culture conditions before analysing their response to standard conditions of glucose-stimulated insulin secretion. The authors report that high glucose, rather than glucose per se, is detrimental for beta cell function. Cells exposed to fatty acids and high glucose exhibited massive fat storage, which was rapidly mobilised upon return to normal conditions. Such fat turnover was instrumental for the preservation of the secretory response in cells experiencing glucotoxicity. The authors conclude that these findings advocate against continuous energy-rich snacking without fasting periods for the preservation of beta cell function.

The influence of bright and dim light on substrate metabolism, energy expenditure and thermoregulation in insulin-resistant individuals depends on time of day

Jan-Frieder Harmsen, Jakob Wefers, Daniel Doligkeit, Luc Schlangen, Bas Dautzenberg, Pascal Rense, Dirk van Moorsel, Joris Hoeks, Esther Moonen-Kornips, Marijke C. M. Gordijn, Wouter D. van Marken Lichtenbelt, Patrick Schrauwen

We spend most of our time indoors under light conditions that are either not as bright as natural daylight or too bright in the evening after sunset. Such suboptimal light conditions are considered to be risk factors for metabolic diseases, with detrimental effects of light exposure at night on sleep quality and glucose metabolism. In this issue, Harmsen and Wefers et al (https://doi.org/10.1007/s00125-021-05643-9) investigate the metabolic impact in insulin-resistant men and women of a 24 h light scheme resembling the natural light/dark cycle, with bright light during daytime and dim light during the evening. They report that the optimised light scheme was beneficial for plasma glucose levels preceding dinner, energy expenditure during the night, and diurnal rhythms in peripheral skin temperature. The authors conclude that these findings provide the rationale to further explore indoor lighting designs to prevent or treat metabolic diseases.